

USSN 09/493,545  
Page 4

*As  
Amended*

21. A composition for the regeneration of articular cartilage said composition comprising an effective amount of an osteochondral graft in combination with an effective amount of BMP-2 effective for the regeneration of said articular cartilage.

**REMARKS**

Claims 1,2,5,8,9 and 12 have been amended and claims 15-21 added. Basis for new claims 15-21 is found in the specification, for example on page 2, lines 2223-30, page 7, lines 29-34 and page 10, lines 27-30. Claims 1-21 remain in the application and are set forth in the Appendix A. Reconsideration of the application is requested.

**Rejections Under 35 USC §112**

Claims 1, 2, 5, 8, 9, and 12, rejected for omitting essential steps, have been amended to recite effective amounts of the composition to regenerate articular cartilage. Basis for the amendments appears in the specification, for example on page 4, lines 14-18. By this amendment Applicants submit that the amount of the composition and duration of administration is clear, thus overcoming the rejection.

Claims 5, 7, 12 and 14 are rejected as indefinite because the claim did not set forth what the abbreviations BIP, GDF, and Vgr-2 represented. The claims have been amend to set forth that BIP represents bone formation -inducing protein. It is Applicants' understanding that MP52 and Vgr-2 were thought to be TGF- $\beta$  related proteins and were given the designation MP52 and Vgr-2, as opposed to abbreviations.

**Rejections Under 35USC §102**

Claims 1-14 are rejected as anticipated by Hattersley et al for teaching compositions comprising BMP-2 and other growth and differentiation factors useful in methods of repairing articular cartilage and inducing cartilage formation. It is Applicants' understanding that Hattersley

USSN 09/493,545

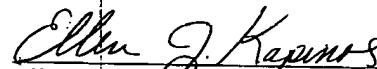
Page 5

discloses the use of BMP-2 together with PTH for the regeneration of articular cartilage (see e.g. column 4, lines 56-66), whereas the present invention is directed to BMPs in the regeneration of articular cartilage (as set forth for example in claims 1 and claim 8). Claims 2 and 9 are directed to methods and compositions for the regeneration of articular cartilage comprising a suitable tissue source in combination with a BMP. Claims dependent thereon specify osteochondral grafts as suitable tissue source. Hattersley does not teach or suggest the use of BMPs in conjunction with such suitable tissue sources to improve healing in the regeneration of articular cartilage.

The examiner contends that Hattersley et al also teaches that protein compositions comprising BMP-2 and BMP-13 are useful in methods of inducing the formation of other types of tissues such as tendons and ligaments. The present claims are distinguished in that the BMP, for example BMP-2, is recited in the claim for the regeneration of articular cartilage regeneration and claims 6 and 13 are directed to a method /composition wherein a further protein, known to induce the formation of tendon or ligament like tissue, is included. The claims of the present invention are not directed to BMP-2 and BMP-13 together for the induction of formation of tendon and ligament tissue.

Reconsideration of the application and entry of the amendments is requested. Should the Examiner believe that a telephonic interview would assist in clarifying any remaining issues, the Examiner is invited to call the undersigned attorney at the telephone number provided below.

Respectfully submitted,



Ellen J. Kapinos  
Reg. No. 32,245  
Attorney for Applicants  
(617) 665-8857  
Correspondence Address:  
Kay Brady  
American Home Products  
Patent Department -2B  
One Campus Drive  
Parsippany, New Jersey 07054

USSN 09/493,545  
Page 6

### Appendix A

1. A method for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.
  
2. A method for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of a tissue source in combination with an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.
  
3. The method of claim 1 wherein said BMP is BMP-2
  
4. The method of claim 2 wherein said BMP is BMP-2.
  
5. A method for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of at least one purified protein selected from the group consisting of Vgr-2, growth and differentiation factors (GDFs), and bone formation-inducing protein( BIP) effective for the regeneration of said articular cartilage.
  
6. The method of claim 1 further comprising a protein which induces the formation of tendon or ligament-like tissue.
  
7. The method of claim 6 wherein said protein which induces the formation of tendon or ligament-like tissue is selected from the group consisting of BMP-12, BMP-13 members of the BMP-12 subfamily and MP52.

USSN 09/493,545

Page 7

8. A composition for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.
9. A composition for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of a tissue source in combination with an effective amount of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.
10. The composition of claim 1 wherein said BMP is BMP-2
11. The composition of claim 2 wherein said BMP is BMP-2.
12. A composition for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an effective amount of at least one purified protein selected from the group consisting of Vgr-2, growth and differentiation factors (GDFs), and bone formation-inducing protein(BIP) effective for the regeneration of said articular cartilage.
13. The composition of claim 1 further comprising a protein which induces the formation of tendon or ligament-like tissue.
14. The composition of claim 6 wherein said protein which induces the formation of tendon or ligament-like tissue is selected from the group consisting of BMP-12, BMP-13 members of the BMP-12 subfamily and MP52.
15. The method of claim 2 wherein said suitable tissue source is osteochondral graft.

USSN 09/493,545  
Page 8

16. The method of claim 15 wherein said osteochondral graft is osteochondral allograft.
17. The method of claim 15 wherein said osteochondral graft is osteochondral autograft.
18. The composition of claim 9 wherein said suitable tissue source is osteochondral graft.
19. The composition of claim 18 wherein said osteochondral graft is osteochondral allograft.
20. The composition of claim 18 wherein said osteochondral graft is osteochondral autograft.
21. A composition for the regeneration of articular cartilage said composition comprising an effective amount of an osteochondral graft in combination with an effective amount of BMP-2 effective for the regeneration of said articular cartilage.